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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/718,425	11/24/2000	Oren Becker	24460	1582

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EXAMINER	
TAYLOR, JANELL E	

ART UNIT	PAPER NUMBER
1634	8

DATE MAILED: 08/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/718,425	BECKER ET AL.	
	Examiner	Art Unit	
	Taylor, Janell	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the restriction requirement is improper because it omits an appropriate explanation as to the existence of a serious burden. Applicant also states that an examination of all the claims in this application would not pose a serious burden because a search of any one of invention I-IV would require searching the prior art areas appropriate to the other groups. This is not found persuasive because, first of all, the restriction requirement clearly laid out an explanation as to why searching all groups would pose a serious burden. The reasons are reproduced below, supra. Secondly, Applicant's contention that searching one group would necessitate searching all groups is unfounded. Each group belongs to a different class, and different searches would have to be performed for each group separately. Finally, Applicant argues that they have paid a full filing fee and that they will have to pay duplicative fees if the inventions aren't examined together. This is not, however, considered a valid reason for not setting forth an appropriate restriction.

> *1. Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the amino acid may be made by a materially different process; i.e., the product may occur in nature or be synthesized by one of the multiple amino acid synthesis methods known in the art.*
> *2. Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a nucleic acid and an amino acid, which have different functions, i.e., the nucleic acid codes for amino acids and the amino acids are used to create proteins, which are used for various purposes in the cell, including enzymatic functions, structural functions, etc. The nucleic acid is capable of functioning to code for a peptide without the peptide being present, and can be used by the practitioner to create probes, primers, and for diagnostic purposes without the presence of the peptide.*

Furthermore, the peptide is capable of functioning without the nucleic acid being present in the cell, as well as being useful to the practitioner.
The inventions are distinct, each from the other because of the following reasons:
3. Inventions I and IV are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case of groups I and IV, the process may be practiced by another materially different apparatus. For instance, the apparatus of Group IV teaches different memories, which are not all necessary for practicing the method of Group I. Furthermore, the apparatus is useable with methods other than those presented in Group I. For instance, the apparatus may be used to confirm an already-known amino acid structure, in which case the steps of the method would be different.
4. Inventions II, III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to different products and an apparatus. They each have different modes of operation and different effects. The amino acid and nucleic acid do not have the same function or mode of operation as the apparatus.
5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.
6. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II or III or IV, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

1. Claim 1 is objected to because of the following informalities: improper punctuation. There is a period at the end of step (f) in claim 1, where it is believed there should be a semicolon. Appropriate correction is required.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-5, 9-17, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Dahiyat et al. (Protein Science, 1996, Vol. 5, 895-903).

Dahiyat teaches protein design automation. Specifically, they teach "We have conceived and implemented a cyclical protein design strategy that couples theory, computation, and experimental testing. The combinatorially large number of possible sequences and the incomplete understanding of the factors that control protein structure are the primary obstacles in protein design. Our protein design automation algorithm objectively predicts protein sequences likely to achieve a desired fold. Using a rotamer description of the side chains, we implanted a fast discrete search algorithm based on the Dead End Elimination Theorem to rapidly find the globally optimal sequence in its optimal geometry from the vast number of possible solutions. Rotamer sequences were scored for steric complementarity using a van der Walls potential. A Monte Carlo search was then executed, starting at the optimal sequence, in order to find other high-scoring sequences. As a test of the design methodology, high-scoring sequences were found for the buried hydrophobic residues of a homodimeric coiled coil based on GCN4-p1. The corresponding peptides were synthesized and characterized by DC spectroscopy and size exclusion chromatography...A quantitative structure activity relation analysis was performed on the designed peptides, and a significant correlation was found with surface area burial. Incorporation of a buried surface area potential in the scoring of sequences greatly improved the correlation between predicted and measured stabilities and demonstrated experimental feedback in a complete design cycle." (Abstract). Specifically, Dahiyat also teaches that the PDA side-chain selection algorithm requires as input a backbone structure defining the desired fold. Also taught is that "using a rotamer description of side chains, an optimal sequence for a backbone can be found

by screening all possible sequences of rotamers, where each backbone position can be occupied by each amino acid and all its possible rotameric states." (page 896). (This corresponds to steps (a) through (d) of claim 1). Also taught is "following DEE optimization, a rank-ordered list of sequences is generated by a Monte Carlo search in the neighborhood of the DEE solution...random positions are changed to other rotamers, and the new sequence energy is calculated. If the new sequence energy meets the Boltzmann criteria for acceptance, it is used as the starting point for another jump...after a predetermined number of jumps, the best scoring sequences are output as a rank-ordered list." (Page 897). (This corresponds to step (e) of claim 1). Also taught is that simpler structure measures, such as buried atoms, were used to resolve the structure of the amino acid. (page 899) (this corresponds to step (f) of claim 1). Dahiyat also teaches using hydrophobic and hydrophilic positions to determine the structure. (Page 897). In regards to claims 8, 10, and 11, since all positions are selected from the entire group of amino acids, these claims are fully anticipated.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dahiyat, as applied to claims above, and further in view of Hurley et al. (J. Mol. Biol., Vo. 224, 1992, pages 1143-1159).

As disclosed above, Dahiyat teaches protein design automation. Specifically, they teach "We have conceived and implemented a cyclical protein design strategy that couples theory, computation, and experimental testing. The combinatorially large number of possible sequences and the incomplete understanding of the factors that control protein structure are the primary obstacles in protein design. Our protein design automation algorithm objectively predicts protein sequences likely to achieve a desired fold. Using a rotamer description of the side chains, we implanted a fast discrete search algorithm based on the Dead End Elimination Theorem to rapidly find the globally optimal sequence in its optimal geometry from the vast number of possible solutions. Rotamer sequences were scored for steric complementarity using a van der Walls potential. A Monte Carlo search was then executed, starting at the optimal sequence, in order to find other high-scoring sequences. As a test of the design methodology, high-scoring sequences were found for the buried hydrophobic residues of a homodimeric coiled coil based on GCN4-p1. The corresponding peptides were synthesized and characterized by DC spectroscopy and size exclusion chromatography...A quantitative structure activity relation analysis was performed on the designed peptides, and a significant correlation was found with surface area burial. Incorporation of a buried surface area potential in the scoring of sequences greatly improved the correlation between predicted and measured stabilities and demonstrated experimental feedback in a complete design cycle." (Abstract). Specifically, Dahiyat also teaches that the PDA side-chain selection algorithm requires as input a backbone structure defining the desired fold. Also taught is that "using a rotamer description of side chains, an optimal

sequence for a backbone can be found by screening all possible sequences of rotamers, where each backbone position can be occupied by each amino acid and all its possible rotameric states." (page 896). (This corresponds to steps (a) through (d) of claim 1). Also taught is "following DEE optimization, a rank-ordered list of sequences is generated by a Monte Carlo search in the neighborhood of the DEE solution...random positions are changed to other rotamers, and the new sequence energy is calculated. If the new sequence energy meets the Boltzmann criteria for acceptance, it is used as the starting point for another jump...after a predetermined number of jumps, the best scoring sequences are output as a rank-ordered list." (Page 897). (This corresponds to step (e) of claim 1). Also taught is that simpler structure measures, such as buried atoms, were used to resolve the structure of the amino acid. (page 899) (this corresponds to step (f) of claim 1).

Dahiyat does not teach that the solvent is substantially water.

Hurley et al. teaches design and structural analysis of alternative hydrophobic core packing arrangements in bacteriophage T4 lysozyme. Particularly, they teach that: "in order to calculate stability changes in aqueous solution, the changes in free energies of transfer of the folded and unfolded states between water and vacuum must be obtained." (Page 1146).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Dahiyat and those of Hurley. As Hurley taught, it would have been obvious to determine the structure of an amino acid in water because it would have allowed for the calculation of stability change. Also, water would have

been a common solvent for the amino acid structures to be found in naturally, and therefore would have been obvious to use as it would have allowed for the closest proximation to nature. Furthermore, water would have been an obvious solvent due to its neutral pH, low cost, and easy availability.

Conclusion

Any inquiries of a general nature relating to this application, including information on IDS forms, status requests, sequence listings, etc. should be directed to the Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janell Taylor Cleveland, whose telephone number is (703) 305-0273.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (703) 308-1152.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1634 via the PTO Fax Center using (703) 872-9306 or 872-9307 (after final). The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989.)

Janell Taylor Cleveland

July 31, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600